

PATENT COOPERATION TREATY

PCT

NOTIFICATION OF THE RECORDING OF A CHANGE

(PCT Rule 92bis.1 and
Administrative Instructions, Section 422)

From the INTERNATIONAL BUREAU

To:

KIDDLE, Simon, J.
Mewburn Ellis
York House
23 Kingsway
London WC2B 6HP
ROYAUME-UNI

Date of mailing (day/month/year) 19 February 2001 (19.02.01)	
Applicant's or agent's file reference SJK/BP5846076	IMPORTANT NOTIFICATION
International application No. PCT/GB00/01030	International filing date (day/month/year) 20 March 2000 (20.03.00)

1. The following indications appeared on record concerning: <input checked="" type="checkbox"/> the applicant <input type="checkbox"/> the inventor <input type="checkbox"/> the agent <input type="checkbox"/> the common representative		
Name and Address UNIVERSITY OF ABERDEEN Research and Innovation 23 St Machar Drive Aberdeen AB24 3RY United Kingdom	State of Nationality GB	State of Residence GB
	Telephone No.	
	Facsimile No.	
	Teleprinter No.	
2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning: <input type="checkbox"/> the person <input checked="" type="checkbox"/> the name <input type="checkbox"/> the address <input type="checkbox"/> the nationality <input type="checkbox"/> the residence		
Name and Address THE UNIVERSITY COURT OF THE UNIVERSITY OF ABERDEEN Research and Innovation 23 St Machar Drive Aberdeen AB24 3RY United Kingdom	State of Nationality GB	State of Residence GB
	Telephone No.	
	Facsimile No.	
	Teleprinter No.	
3. Further observations, if necessary:		
4. A copy of this notification has been sent to: <div style="display: flex; justify-content: space-between;"> <div> <input checked="" type="checkbox"/> the receiving Office <input type="checkbox"/> the International Searching Authority <input checked="" type="checkbox"/> the International Preliminary Examining Authority </div> <div> <input type="checkbox"/> the designated Offices concerned <input checked="" type="checkbox"/> the elected Offices concerned <input type="checkbox"/> other: </div> </div>		

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No.: (41-22) 740.14.35	Authorized officer Eugénia Santos Telephone No.: (41-22) 338.83.38
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PATENT COOPERATION TREATY

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NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Commissioner
 US Department of Commerce
 United States Patent and Trademark
 Office, PCT
 2011 South Clark Place Room
 CP2/5C24
 Arlington, VA 22202
 ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 22 November 2000 (22.11.00)	
International application No. PCT/GB00/01030	Applicant's or agent's file reference SJK/BP5846076
International filing date (day/month/year) 20 March 2000 (20.03.00)	Priority date (day/month/year) 19 March 1999 (19.03.99)
Applicant MELVIN, William et al	

1. The designated Office is hereby notified of its election made:

☒ in the demand filed with the International Preliminary Examining Authority on:

19 October 2000 (19.10.00)

☐ in a notice effecting later election filed with the International Bureau on:
2. The election ☒ was
☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No.: (41-22) 740.14.35	Authorized officer Zakaria EL KHODARY Telephone No.: (41-22) 338.83.38
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PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference SJK/BP5846076	FOR FURTHER ACTION <small>see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.</small>	
International application No. PCT/GB 00/ 01030	International filing date (day/month/year) 20/03/2000	(Earliest) Priority Date (day/month/year) 19/03/1999
Applicant UNIVERSITY OF ABERDEEN et al.		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 3 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

☐ contained in the international application in written form.

☐ filed together with the international application in computer readable form.

☒ furnished subsequently to this Authority in written form.

☒ furnished subsequently to this Authority in computer readable form.

☒ the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☒ the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. ☐ **Certain claims were found unsearchable** (See Box I).

3. ☐ **Unity of invention is lacking** (see Box II).

4. With regard to the **title**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No.

☐ as suggested by the applicant.

☐ because the applicant failed to suggest a figure.

☐ because this figure better characterizes the invention.

☒ Non of the figures.

INTERNATIONAL SEARCH REPORT

International Application No

T/GB 00/01030

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07K16/40 C12N5/06 A61K47/48 G01N33/573 G01N33/574
G01N33/577 A61P35/00 C12N9/02

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07K C12N G01N A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

WPI Data, PAJ, MEDLINE, BIOSIS, EMBASE, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 97 12246 A (UNIVERSITY OF ABERDEEN) 3 April 1997 (1997-04-03) claims 1-26 ---	1-19, 21-25
X	MURRAY G ET AL: "Tumor-specific expression of cytochrome P450 CYP1B1." CANCER RESEARCH (1997) 57 3026-31, XP002106430 page 3027, right-hand column, line 5 - line 13 ----- -/-	1-18, 20-25

☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

* Special categories of cited documents :

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- *&* document member of the same patent family

Date of the actual completion of the international search

22 June 2000

Date of mailing of the international search report

06/07/2000

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
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Authorized officer

Le Flao, K

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	TAILOR, G. ET AL: "Detection of cytochrome P450 CYP1B1 in human tumours using monoclonal antibodies against a C-terminal decapeptide." HUMAN & EXPERIMENTAL TOXICOLOGY, (SEPT., 1998) VOL. 17, NO. 9, PP. 534. MEETING INFO.: PROCEEDINGS OF THE BRITISH TOXICOLOGY SOCIETY ANNUAL CONGRESS GUILFORD, ENGLAND, UK APRIL 19-22, 1998 BRITISH TOXICOLOGICAL SOCIETY. , XP000914865 abstract ---	1-18, 20-25
X	TANG Y M ET AL: "Development of an antipeptide antibody that binds to the C-terminal region of human CYP1B1." DRUG METABOLISM AND DISPOSITION, (1999 FEB) 27 (2) 274-80. , XP000914872 abstract page 276, left-hand column, line 15 - line 28 ---	1-18
A	MCKAY J ET AL: "Expression of cytochrome P450 CYP1B1 in breast cancer" FEBS LETTERS (1995) 374 270-2, XP000615313 page 271, right-hand column, line 15 - line 24; figure 4 -----	1-25

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

T/GB 00/01030

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9712246 A	03-04-1997	AU 7090396 A EP 0856157 A JP 11512818 T	17-04-1997 05-08-1998 02-11-1999
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REC'D 30 JUL 2001

V/IPO

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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)


Applicant's or agent's file reference SJK/BP5846076	FOR FURTHER ACTION		See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/GB00/01030	International filing date (day/month/year) 20/03/2000	Priority date (day/month/year) 19/03/1999	
International Patent Classification (IPC) or national classification and IPC C07K16/40			
Applicant THE UNIVERSITY OF COURT OF THE UNIVERSITY OF ABERDEEN			

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 8 sheets, including this cover sheet.
- ☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of 4 sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☒ Certain defects in the international application
- VIII ☒ Certain observations on the international application

Date of submission of the demand 19/10/2000	Date of completion of this report 02.07.2001
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Giry, M Telephone No. +49 89 2399 7328



**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/GB00/01030

I. Basis of the report

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

Description, pages:

1-37 as originally filed

Claims, No.:

1-25 as received on 03/05/2001 with letter of 01/05/2001

Drawings, sheets:

1/4-4/4 as originally filed

Sequence listing part of the description, pages:

1-6, filed with the letter of 22.05.2000

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☒ furnished subsequently to this Authority in written form.
- ☒ furnished subsequently to this Authority in computer readable form.
- ☒ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☒ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/GB00/01030

- ☐ the description, pages:
☐ the claims, Nos.:
☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-25
	No:	Claims	
Inventive step (IS)	Yes:	Claims	1-25
	No:	Claims	
Industrial applicability (IA)	Yes:	Claims	1-25
	No:	Claims	

2. Citations and explanations
see separate sheet

VII. Certain defects in the international application

The following defects in the form or contents of the international application have been noted:
see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:
see separate sheet

Re Item V

Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1 - Reference is made to the following documents :

D1 : WO 97 12246 A, 3 April 1997

D2 : Murray G et al. : 'Tumor-specific expression of cytochrome P450 CYP1B1.'
Cancer Res. (1997) 57 : 3026-31

D3 : Tailor G et al. : 'Detection of cytochrome P450 CYP1B1 in human tumours
using monoclonal antibodies against a C-terminal decapeptide.' Human &
Experimental Toxicology (Sept., 1998) Vol. 17, No. 9, pp. 534. Meeting Info.:
Proceedings of the British Toxicology Society Annual Congress Guilford,
England, UK Apr. 19-22, 1998 British Toxicological Society

2 - Novelty - Art. 33(1) and (2) PCT :

Neither a peptide consisting of the amino acid sequence given in claim 1, nor an antibody raised against said peptide or an antigenic fragment thereof are disclosed in the available prior art documents. The subject-matter of claims 1-25 can therefore be regarded as novel.

3 - Inventive step - Art. 33(1) and (3) PCT :

- 3.1 Document D1 discloses methods for the identification of tumour cells using an antibody directed to the tumour-specific form of cytochrome P450, the CYP1B1 protein (p. 3, lines 1-8 ; p. 21, claims 1-2). Such methods include immunohistochemistry, Western blot analysis, and immunoassays such as antibody capture assays, two-antibody sandwich assays, and antigen capture assays (p. 8, lines 19-20 ; p. 21-22, claims 3-19) and are realized utilizing polyclonal or monoclonal antibodies raised to 15-mer peptides corresponding to epitopes of the human CYP1B1 protein (p. 9, lines 22-32 ; p. 22, claims 16-19). These immunohistochemistry analysis are performed in the case of different types

of cancers developed in a range of different anatomical sites such as bladder, breast, colon, kidney, lung, oesophagus, ovary, etc. (p. 5, lines 20-27 ; p. 22, claim 20). Document D1 also mentions the important consequences for both diagnosis and treatment of cancer of the tumour-specific CYP1B1 protein (p. 7, lines 7-8).

- 3.2 Document D2 also describes the tumour-specific expression analysis in lymphoblastoid cells of the CYP1B1 protein using an antibody raised to a peptide specific for this protein and reports on immunohistochemistry analysis performed in a range of malignant tumours (p. 3028, Table 1), suggesting the development of methods of cancer diagnosis based on the identification of CYP1B1 in tumour cells (Abstract, lines, 3-4, 7-8, 14-15). The polyclonal anti-CYP1B1 antibody was generated using a synthetic peptide corresponding to the amino acid residues 332-345 of the human CYP1B1 sequence conjugated to the immunogenic carrier keyhole limpet haemocyanin (p. 3026, col. 2, 5 last lines to p. 3027, col. 1, line 10 ; p. 3027, col. 2, lines 7-13).
- 3.3 Document D3 teaches the detection in immunohistochemical analysis of the tumour specific cytochrome P450 form CYP1B1 in human tumours using two monoclonal antibodies (LDS100 and LDS101) generated against decapeptides located in the C-terminal part of CYP1B1 and suggests the use of these monoclonal antibodies for the diagnostic of cancer (the whole document).
- 3.4 The present application differs from document D1 which is considered to represent the closest prior art document solely by the peptides used to raise antibodies directed to the tumour specific cytochrome P450 CYP1B1. The problem to be solved by the invention can therefore be seen in providing alternative antibodies specific for the protein CYP1B1.
- 3.5 The subject-matter of independent claims 1 and 7 concerns methods of "making" and "producing" an antibody using 15-mer peptides consisting of the amino acid residues 422-436 and 437-451 of the human CYP1B1 protein or an antigenic fragment thereof.
- As there is no disclosure or suggestion of the two peptides as claimed in claim 1 in either documents D1, D2 and D3 or any of the other documents cited in the

International Search Report, the subject-matter of claim 1 cannot be considered as obvious, given the available prior art. Moreover, in contrast to other CYP1B1 peptides tested, only the said peptides referred to in claim 1 appear to be able to provide an immune response as mentioned in Table 1, p. 18 of the description. The subject-matter of independent claims 1 and 7 therefore appears to involve an inventive step.

- 3.6 Claims 2-6 are dependent on claim 1 and claims 8-9 are dependent on claim 7, and as such also meet the requirements of the PCT as regards inventive step.
- 3.7 The description provides evidence that experiments carried out using antibodies raised using said CYP1B1 peptides according to independent claim 10 are particularly useful for carrying out immunoreactivity assays, *e.g.*, for detecting breast cancer cells in samples, and do not cross react with CYP1A1 (p. 25-32). Therefore, the subject-matter of claims 10-17 can be considered as involving an inventive step.
- 3.8 Since antibodies raised against said CYP1B1 epitopes can be regarded as potentially useful as therapeutics, as suggested on p. 35, lines 1-21 of the description, the subject-matter of independent claims 18 and 19 can be seen as involving an inventive step.
- 3.9 The subject-matter of independent claim 20 can be regarded as involving an inventive step for the reasons given under point 3.5 above.
- 3.10 The assay method based on an antibody according to claims 10 to 17, subject-matter of claims 21-25 can be regarded as involving an inventive step for the reasons given under point 3.7 above.

4 - Industrial applicability - Art. 33(1) and (4) PCT :

For the assessment of the present claims 18-19 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO,

for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

Re Item VII

Certain defects in the international application

The vague and imprecise statement "scope of the invention" on p. 11, lines 11-12 of the description implies that the subject-matter for which protection is sought may be different to that defined by the claims, thereby resulting in lack of clarity when used to interpret them. Such expressions are not allowed and should have been deleted (Art. 6 PCT, PCT Guidelines III-4.3a).

Re Item VIII

Certain observations on the international application

1. It was previously objected that the phrase "having obtained a hybridoma by the method of claim 6" does not introduce any limiting technical feature in claim 7, rendering the subject-matter of claim 7 unclear. As the Applicant's Representative stressed, it is understood that claim 7 is directed to the subsequent activity of culturing the hybridoma obtained by the method of claim 6 and isolating the antibody thus produced. Therefore, in order to make clear that independent claim 7 relates to another method which is directed to the production of an antibody, it appears that it should have been appropriate to incorporate steps (a), (b) and (c) comprised in the method of claim 6 to replace the expression "culturing a hybridoma found in step (c)", and to designate as a step (d) the step of isolating the antibody produced in step (c) (Art. 6 PCT).
2. Claim 15 concerns "the antibody of claim 13" *per se* since the method used to obtain it has no limiting effect on the scope of the claim (Art. 6 PCT). Therefore,

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/GB00/01030

claims 15 and 13 appear to relate to the same subject-matter. The use of two independent claims covering the same subject-matter renders the set of claims as a whole unclear (Art. 6 PCT) and introduces a lack of conciseness (Rule 6.1(a) PCT ; see also PCT Guidelines III-5.1). Thus, it appears that claim 15 should have been deleted.

INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB 00/01030

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07K16/40 C12N5/06 A61K47/48 G01N33/573 G01N33/574
G01N33/577 A61P35/00 C12N9/02

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07K C12N G01N A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

WPI Data, PAJ, MEDLINE, BIOSIS, EMBASE, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 97 12246 A (UNIVERSITY OF ABERDEEN) 3 April 1997 (1997-04-03) claims 1-26	1-19, 21-25
X	MURRAY G ET AL: "Tumor-specific expression of cytochrome P450 CYP1B1." CANCER RESEARCH (1997) 57 3026-31, XP002106430 page 3027, right-hand column, line 5 - line 13	1-18, 20-25

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents:

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

- "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- "&" document member of the same patent family

Date of the actual completion of the international search

22 June 2000

Date of mailing of the international search report

06/07/2000

Name and mailing address of the ISA

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Authorized officer

Le Flao, K

INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB 00/01030

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	TAILOR, G. ET AL: "Detection of cytochrome P450 CYP1B1 in human tumours using monoclonal antibodies against a C-terminal decapeptide." HUMAN & EXPERIMENTAL TOXICOLOGY, (SEPT., 1998) VOL. 17, NO. 9, PP. 534. MEETING INFO.: PROCEEDINGS OF THE BRITISH TOXICOLOGY SOCIETY ANNUAL CONGRESS GUILFORD, ENGLAND, UK APRIL 19-22, 1998 BRITISH TOXICOLOGICAL SOCIETY. , XP000914865 abstract	1-18, 20-25
X	TANG Y M ET AL: "Development of an antipeptide antibody that binds to the C-terminal region of human CYP1B1." DRUG METABOLISM AND DISPOSITION, (1999 FEB) 27 (2) 274-80. , XP000914872 abstract page 276, left-hand column, line 15 - line 28	1-18
A	MCKAY J ET AL: "Expression of cytochrome P450 CYP1B1 in breast cancer" FEBS LETTERS (1995) 374 270-2, XP000615313 page 271, right-hand column, line 15 - line 24; figure 4	1-25

INTERNATIONAL SEARCH REPORT

information on patent family members

International Application No

PCT/GB 00/01030

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9712246 A	03-04-1997	AU 7090396 A	17-04-1997
		EP 0856157 A	05-08-1998
		JP 11512818 T	02-11-1999
<hr/>			

FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

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CU	Cuba	LC	Saint Lucia	RU	Russian Federation		
CZ	Czech Republic	LI	Licchtenstein	SD	Sudan		
DE	Germany	LK	Sri Lanka	SE	Sweden		
DK	Denmark	LR	Liberia	SG	Singapore		
EE	Estonia						

PATENT COOPERATION TREATY

PCT

NOTIFICATION OF THE RECORDING
OF A CHANGE(PCT Rule 92bis.1 and
Administrative Instructions, Section 422)

From the INTERNATIONAL BUREAU

To:

KIDDLE, Simon, J.
Mewburn Ellis
York House
23 Kingsway
London WC2B 6HP
ROYAUME-UNI

28 FEB 2001

Date of mailing (day/month/year) 19 February 2001 (19.02.01)	IMPORTANT NOTIFICATION
Applicant's or agent's file reference SJK/BP5846076	
International application No. PCT/GB00/01030	International filing date (day/month/year) 20 March 2000 (20.03.00)

1. The following indications appeared on record concerning:

☒ the applicant ☐ the inventor ☐ the agent ☐ the common representative

Name and Address

UNIVERSITY OF ABERDEEN
Research and Innovation
23 St Machar Drive
Aberdeen AB24 3RY
United Kingdom

State of Nationality
GB

State of Residence
GB

Telephone No.

Facsimile No.

Teleprinter No.

2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:

☐ the person ☒ the name ☐ the address ☐ the nationality ☐ the residence

Name and Address

THE UNIVERSITY COURT OF THE
UNIVERSITY OF ABERDEEN
Research and Innovation
23 St Machar Drive
Aberdeen AB24 3RY
United Kingdom

State of Nationality
GB

State of Residence
GB

Telephone No.

Facsimile No.

Teleprinter No.

3. Further observations, if necessary:

4. A copy of this notification has been sent to:

☒ the receiving Office ☐ the designated Offices concerned
☐ the International Searching Authority ☒ the elected Offices concerned
☒ the International Preliminary Examining Authority ☐ other:

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Facsimile No.: (41-22) 740.14.35

Authorized officer

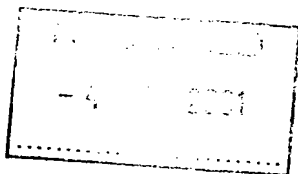
Eugénia Santos

Telephone No.: (41-22) 338.83.38

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:

KIDDLE, Simon J.
MEWBURN ELLIS
York House
23 Kingsway
London WC2B 6HP
GRANDE BRETAGNE



PCT

NOTIFICATION OF TRANSMITTAL OF
THE INTERNATIONAL PRELIMINARY
EXAMINATION REPORT

(PCT Rule 71.1)

Date of mailing
(day/month/year) 02.07.2001

Applicant's or agent's file reference
SJK/BP5846076

IMPORTANT NOTIFICATION

International application No.
PCT/GB00/01030

International filing date (day/month/year)
20/03/2000

Priority date (day/month/year)
19/03/1999

Applicant
UNIVERSITY OF COURT OF THE UNIVERSITY OF ABERDEEN

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.
2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.
3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

4. REMINDER

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

Name and mailing address of the IPEA/



European Patent Office
D-80298 Munich
Tel. +49 89 2399 - 0 Tx: 523656 epmu d
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Authorized officer

Neumann, M

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PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)



Applicant's or agent's file reference SJK/BP5846076	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/GB00/01030	International filing date (day/month/year) 20/03/2000	Priority date (day/month/year) 19/03/1999
International Patent Classification (IPC) or national classification and IPC C07K16/40		
Applicant UNIVERSITY OF COURT OF THE UNIVERSITY OF ABERDEEN		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 8 sheets, including this cover sheet.
- ☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of 4 sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☒ Certain defects in the international application
- VIII ☒ Certain observations on the international application

Date of submission of the demand 19/10/2000	Date of completion of this report 02.07.2001
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Giry, M Telephone No. +49 89 2399 7328 

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/GB00/01030

I. Basis of the report

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

Description, pages:

1-37 as originally filed

Claims, No.:

1-25 as received on 03/05/2001 with letter of 01/05/2001

Drawings, sheets:

1/4-4/4 as originally filed

Sequence listing part of the description, pages:

1-6, filed with the letter of 22.05.2000

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☒ furnished subsequently to this Authority in written form.
- ☒ furnished subsequently to this Authority in computer readable form.
- ☒ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☒ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/GB00/01030

- ☐ the description, pages:
- ☐ the claims, Nos.:
- ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-25
	No:	Claims	
Inventive step (IS)	Yes:	Claims	1-25
	No:	Claims	
Industrial applicability (IA)	Yes:	Claims	1-25
	No:	Claims	

2. Citations and explanations
see separate sheet

VII. Certain defects in the international application

The following defects in the form or contents of the international application have been noted:
see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:
see separate sheet

Re Item V

Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1 - Reference is made to the following documents :

D1 : WO 97 12246 A, 3 April 1997

D2 : Murray G et al. : 'Tumor-specific expression of cytochrome P450 CYP1B1.' Cancer Res. (1997) 57 : 3026-31

D3 : Tailor G et al. : 'Detection of cytochrome P450 CYP1B1 in human tumours using monoclonal antibodies against a C-terminal decapeptide.' Human & Experimental Toxicology (Sept., 1998) Vol. 17, No. 9, pp. 534. Meeting Info.: Proceedings of the British Toxicology Society Annual Congress Guilford, England, UK Apr. 19-22, 1998 British Toxicological Society

2 - Novelty - Art. 33(1) and (2) PCT :

Neither a peptide consisting of the amino acid sequence given in claim 1, nor an antibody raised against said peptide or an antigenic fragment thereof are disclosed in the available prior art documents. The subject-matter of claims 1-25 can therefore be regarded as novel.

3 - Inventive step - Art. 33(1) and (3) PCT :

- 3.1 Document D1 discloses methods for the identification of tumour cells using an antibody directed to the tumour-specific form of cytochrome P450, the CYP1B1 protein (p. 3, lines 1-8 ; p. 21, claims 1-2). Such methods include immunohistochemistry, Western blot analysis, and immunoassays such as antibody capture assays, two-antibody sandwich assays, and antigen capture assays (p. 8, lines 19-20 ; p. 21-22, claims 3-19) and are realized utilizing polyclonal or monoclonal antibodies raised to 15-mer peptides corresponding to epitopes of the human CYP1B1 protein (p. 9, lines 22-32 ; p. 22, claims 16-19). These immunohistochemistry analysis are performed in the case of different types

of cancers developed in a range of different anatomical sites such as bladder, breast, colon, kidney, lung, oesophagus, ovary, etc. (p. 5, lines 20-27 ; p. 22, claim 20). Document D1 also mentions the important consequences for both diagnosis and treatment of cancer of the tumour-specific CYP1B1 protein (p. 7, lines 7-8).

- 3.2 Document D2 also describes the tumour-specific expression analysis in lymphoblastoid cells of the CYP1B1 protein using an antibody raised to a peptide specific for this protein and reports on immunohistochemistry analysis performed in a range of malignant tumours (p. 3028, Table 1), suggesting the development of methods of cancer diagnosis based on the identification of CYP1B1 in tumour cells (Abstract, lines, 3-4, 7-8, 14-15). The polyclonal anti-CYP1B1 antibody was generated using a synthetic peptide corresponding to the amino acid residues 332-345 of the human CYP1B1 sequence conjugated to the immunogenic carrier keyhole limpet haemocyanin (p. 3026, col. 2, 5 last lines to p. 3027, col. 1, line 10 ; p. 3027, col. 2, lines 7-13).
- 3.3 Document D3 teaches the detection in immunohistochemical analysis of the tumour specific cytochrome P450 form CYP1B1 in human tumours using two monoclonal antibodies (LDS100 and LDS101) generated against decapeptides located in the C-terminal part of CYP1B1 and suggests the use of these monoclonal antibodies for the diagnostic of cancer (the whole document).
- 3.4 The present application differs from document D1 which is considered to represent the closest prior art document solely by the peptides used to raise antibodies directed to the tumour specific cytochrome P450 CYP1B1. The problem to be solved by the invention can therefore be seen in providing alternative antibodies specific for the protein CYP1B1.
- 3.5 The subject-matter of independent claims 1 and 7 concerns methods of "making" and "producing" an antibody using 15-mer peptides consisting of the amino acid residues 422-436 and 437-451 of the human CYP1B1 protein or an antigenic fragment thereof.
- As there is no disclosure or suggestion of the two peptides as claimed in claim 1 in either documents D1, D2 and D3 or any of the other documents cited in the

International Search Report, the subject-matter of claim 1 cannot be considered as obvious, given the available prior art. Moreover, in contrast to other CYP1B1 peptides tested, only the said peptides referred to in claim 1 appear to be able to provide an immune response as mentioned in Table 1, p. 18 of the description. The subject-matter of independent claims 1 and 7 therefore appears to involve an inventive step.

- 3.6 Claims 2-6 are dependent on claim 1 and claims 8-9 are dependent on claim 7, and as such also meet the requirements of the PCT as regards inventive step.
- 3.7 The description provides evidence that experiments carried out using antibodies raised using said CYP1B1 peptides according to independent claim 10 are particularly useful for carrying out immunoreactivity assays, *e.g.*, for detecting breast cancer cells in samples, and do not cross react with CYP1A1 (p. 25-32). Therefore, the subject-matter of claims 10-17 can be considered as involving an inventive step.
- 3.8 Since antibodies raised against said CYP1B1 epitopes can be regarded as potentially useful as therapeutics, as suggested on p. 35, lines 1-21 of the description, the subject-matter of independent claims 18 and 19 can be seen as involving an inventive step.
- 3.9 The subject-matter of independent claim 20 can be regarded as involving an inventive step for the reasons given under point 3.5 above.
- 3.10 The assay method based on an antibody according to claims 10 to 17, subject-matter of claims 21-25 can be regarded as involving an inventive step for the reasons given under point 3.7 above.

4 - Industrial applicability - Art. 33(1) and (4) PCT :

For the assessment of the present claims 18-19 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO,

for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

Re Item VII

Certain defects in the international application

The vague and imprecise statement "scope of the invention" on p. 11, lines 11-12 of the description implies that the subject-matter for which protection is sought may be different to that defined by the claims, thereby resulting in lack of clarity when used to interpret them. Such expressions are not allowed and should have been deleted (Art. 6 PCT, PCT Guidelines III-4.3a).

Re Item VIII

Certain observations on the international application

1. It was previously objected that the phrase "having obtained a hybridoma by the method of claim 6" does not introduce any limiting technical feature in claim 7, rendering the subject-matter of claim 7 unclear. As the Applicant's Representative stressed, it is understood that claim 7 is directed to the subsequent activity of culturing the hybridoma obtained by the method of claim 6 and isolating the antibody thus produced. Therefore, in order to make clear that independent claim 7 relates to another method which is directed to the production of an antibody, it appears that it should have been appropriate to incorporate steps (a), (b) and (c) comprised in the method of claim 6 to replace the expression "culturing a hybridoma found in step (c)", and to designate as a step (d) the step of isolating the antibody produced in step (c) (Art. 6 PCT).
2. Claim 15 concerns "the antibody of claim 13" *per se* since the method used to obtain it has no limiting effect on the scope of the claim (Art. 6 PCT). Therefore,

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/GB00/01030

claims 15 and 13 appear to relate to the same subject-matter. The use of two independent claims covering the same subject-matter renders the set of claims as a whole unclear (Art. 6 PCT) and introduces a lack of conciseness (Rule 6.1(a) PCT ; see also PCT Guidelines III-5.1). Thus, it appears that claim 15 should have been deleted.

Claims:

1. A method of making an antibody that specifically binds to cytochrome P450 CYP1B1, the method comprising raising the antibody using a peptide consisting of an amino acid sequence VNQWSVNHDVPVKWPN or PExFDPARFLDKDGy, where x is D or N and y is L or F, or an antigenic fragment thereof.
5
2. The method of claim 1 wherein the peptide consists of 3 to 10 amino acids.
10
3. The method of claim 1 or claim 2 wherein the peptide consists of 3 to 6 amino acids.
4. The method of any one of claims 1 to 3 wherein the peptide is conjugated to an immunogenic carrier.
15
5. The method of any one of the preceding claims, wherein the antibody is a monoclonal antibody.
20
6. The method of claim 5 wherein the monoclonal antibody is as obtainable by a method which comprises:
 - (a) immunising an animal with the peptide conjugated to an immunogenic carrier;
 - 25 (b) sacrificing the animal and fusing spleen cells obtained from the animal with myeloma cells to produce one or more hydridomas; and,
 - (c) screening the hybridomas for antibodies capable of binding the peptide.
30
7. A method of producing an antibody having obtained a hybridoma by the method of claim 6, the method comprising culturing a hybridoma found in step (c) and isolating the antibody thus produced.
35

8. The method of claim 7, further comprising conjugating the antibody to an effector.

5 9. The method of claim 8, wherein the effector is a label, a toxin, a drug or prodrug, an enzyme or a transport molecule.

10 10. An antibody which is capable of specifically binding to cytochrome P450 CYP1B1, wherein the antibody recognises an epitope in the cytochrome P450 CYP1B1 protein included within the amino acid sequence VNQWSVNHDPVKWPN or PExFDPARFLDKDGy, where x is D or N and y is L or F.

15 11. The antibody of claim 10, wherein the antibody recognises an epitope of between 3 and 10 amino acids from the amino acid sequences.

20 12. The antibody of claim 10, wherein the antibody recognises an epitope of between 3 and 6 amino acids from the amino acid sequences.

25 13. The antibody of any one of claims 10 to 12, wherein the antibody is a monoclonal antibody.

14. The antibody of any one of claims 10 to 12 which is humanised.

30 15. The antibody of claim 13, wherein the antibody is a monoclonal antibody and is as obtainable by:

(a) immunising an animal with the peptide conjugated to an immunogenic carrier;

35 (b) sacrificing the animal and fusing spleen cells obtained from the animal with myeloma cells to produce one or more hydridomas; and,

(c) screening the hybridomas for antibodies capable of binding the peptide.

5 16. The antibody of any one of claims 10 to 15, wherein the antibody is conjugated to an effector.

10 17. The antibody of claim 16, wherein the effector is a label, a toxin, a drug or prodrug, an enzyme or a transport molecule.

18. An antibody of any one of claims 10 to 17 for use in a method of medical treatment.

15 19. Use of an antibody of any one of claim 10 to 17 for the preparation of a medicament for the treatment of cancer.

20 20. A peptide consisting essentially of amino acid sequence VNQWSVNHDPVKWPN or PExFDPARFLDKDGy wherein x is D or N and y is L or F.

25 21. An assay method for detecting cancer cells present in a sample from a patient, the method comprising contacting a tissue sample from a patient with an antibody of any one of claims 10 to 17, and detecting binding of the antibody to CYP1B1 protein present in the sample as an indication of the presence of cancer cells in the tissue sample.

30 22. The method of claim 21, wherein the step of detecting the binding of the antibody to CYP1B1 protein is carried out using an antibody capture assay, a two-antibody sandwich assay or an antigen capture assay.

35 23. The method of claim 21 or claim 22, wherein the

antibody specific for the CYP1B1 protein is immobilised
on a solid support-based immunoassay.

5 24. The method of any one of claims 21 to 23, wherein
the cancer is breast cancer, colorectal cancer, prostate
cancer, liver cancer or ovarian cancer.

10 25. The method of any one of claims 21 to 24, wherein
said tissue sample is selected from bladder, brain,
breast, colon, connective tissue, kidney, lung, lymph
node, oesophagus, ovary, skin, stomach, testis, and
uterus.

PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY

PCT

NOTIFICATION OF TRANSMITTAL OF
THE INTERNATIONAL SEARCH REPORT
OR THE DECLARATION

(PCT Rule 44.1)

To:

MEWBURN ELLIS
York House
Attn. Kiddle, Simon J.
23 Kingsway
London WC2B 6HP
UNITED KINGDOM

RECEIVED

10 JUL 2000

Date of mailing
(day/month/year)

06/07/2000

Applicant's or agent's file reference

SJK/BP5846076

FOR FURTHER ACTION

See paragraphs 1 and 4 below

International application No.

PCT/GB 00/ 01030

International filing date
(day/month/year)

20/03/2000

Applicant

UNIVERSITY OF ABERDEEN et al.

1. ☒ The applicant is hereby notified that the International Search Report has been established and is transmitted herewith.

Filing of amendments and statement under Article 19:

The applicant is entitled, if he so wishes, to amend the claims of the International Application (see Rule 46):

When? The time limit for filing such amendments is normally 2 months from the date of transmittal of the International Search Report; however, for more details, see the notes on the accompanying sheet.

Where? Directly to the International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland
Fascimile No.: (41-22) 740.14.35

For more detailed instructions, see the notes on the accompanying sheet.

2. ☐ The applicant is hereby notified that no International Search Report will be established and that the declaration under Article 17(2)(a) to that effect is transmitted herewith.

RECORDS ENT'D
RECORDS SEEN
DIARY ENT'D
RENEWAL ENT'D X
ALREADY ENT'D

3. ☐ With regard to the protest against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:

☐ the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.

☐ no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

4. **Further action(s):** The applicant is reminded of the following:

Shortly after **18 months** from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in Rules 90bis.1 and 90bis.3, respectively, before the completion of the technical preparations for international publication.

Within **19 months** from the priority date, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase until 30 months from the priority date (in some Offices even later).

Within **20 months** from the priority date, the applicant must perform the prescribed acts for entry into the national phase before all designated Offices which have not been elected in the demand or in a later election within 19 months from the priority date or could not be elected because they are not bound by Chapter II.

Name and mailing address of the International Searching Authority



European Patent Office, P.B. 5818 Patentlaan 2
NL-2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Nina Vercio

These Notes are intended to give the basic instructions concerning the filing of amendments under article 19. The Notes are based on the requirements of the Patent Cooperation Treaty, the Regulations and the Administrative Instructions under that Treaty. In case of discrepancy between these Notes and those requirements, the latter are applicable. For more detailed information, see also the PCT Applicant's Guide, a publication of WIPO.

In these Notes, "Article", "Rule", and "Section" refer to the provisions of the PCT, the PCT Regulations and the PCT Administrative Instructions respectively.

INSTRUCTIONS CONCERNING AMENDMENTS UNDER ARTICLE 19

The applicant has, after having received the international search report, one opportunity to amend the claims of the international application. It should however be emphasized that, since all parts of the international application (claims, description and drawings) may be amended during the international preliminary examination procedure, there is usually no need to file amendments of the claims under Article 19 except where, e.g. the applicant wants the latter to be published for the purposes of provisional protection or has another reason for amending the claims before international publication. Furthermore, it should be emphasized that provisional protection is available in some States only.

What parts of the international application may be amended?

Under Article 19, only the claims may be amended.

During the international phase, the claims may also be amended (or further amended) under Article 34 before the International Preliminary Examining Authority. The description and drawings may only be amended under Article 34 before the International Examining Authority.

Upon entry into the national phase, all parts of the international application may be amended under Article 28 or, where applicable, Article 41.

When?

Within 2 months from the date of transmittal of the international search report or 16 months from the priority date, whichever time limit expires later. It should be noted, however, that the amendments will be considered as having been received on time if they are received by the International Bureau after the expiration of the applicable time limit but before the completion of the technical preparations for international publication (Rule 46.1).

Where not to file the amendments?

The amendments may only be filed with the International Bureau and not with the receiving Office or the International Searching Authority (Rule 46.2).

Where a demand for international preliminary examination has been/is filed, see below.

How?

Either by cancelling one or more entire claims, by adding one or more new claims or by amending the text of one or more of the claims as filed.

A replacement sheet must be submitted for each sheet of the claims which, on account of an amendment or amendments, differs from the sheet originally filed.

All the claims appearing on a replacement sheet must be numbered in Arabic numerals. Where a claim is cancelled, no renumbering of the other claims is required. In all cases where claims are renumbered, they must be renumbered consecutively (Administrative Instructions, Section 205(b)).

The amendments must be made in the language in which the international application is to be published.

What documents must/may accompany the amendments?

Letter (Section 205(b)):

The amendments must be submitted with a letter.

The letter will not be published with the international application and the amended claims. It should not be confused with the "Statement under Article 19(1)" (see below, under "Statement under Article 19(1)").

The letter must be in English or French, at the choice of the applicant. However, if the language of the international application is English, the letter must be in English; if the language of the international application is French, the letter must be in French.

The letter must indicate the differences between the claims as filed and the claims as amended. It must, in particular, indicate, in connection with each claim appearing in the international application (it being understood that identical indications concerning several claims may be grouped), whether

- (i) the claim is unchanged;
- (ii) the claim is cancelled;
- (iii) the claim is new;
- (iv) the claim replaces one or more claims as filed;
- (v) the claim is the result of the division of a claim as filed.

The following examples illustrate the manner in which amendments must be explained in the accompanying letter:

1. [Where originally there were 48 claims and after amendment of some claims there are 51]:
"Claims 1 to 29, 31, 32, 34, 35, 37 to 48 replaced by amended claims bearing the same numbers; claims 30, 33 and 36 unchanged; new claims 49 to 51 added."
2. [Where originally there were 15 claims and after amendment of all claims there are 11]:
"Claims 1 to 15 replaced by amended claims 1 to 11."
3. [Where originally there were 14 claims and the amendments consist in cancelling some claims and in adding new claims]:
"Claims 1 to 6 and 14 unchanged; claims 7 to 13 cancelled; new claims 15, 16 and 17 added." or
"Claims 7 to 13 cancelled; new claims 15, 16 and 17 added; all other claims unchanged."
4. [Where various kinds of amendments are made]:
"Claims 1-10 unchanged; claims 11 to 13, 18 and 19 cancelled; claims 14, 15 and 16 replaced by amended claim 14; claim 17 subdivided into amended claims 15, 16 and 17; new claims 20 and 21 added."

"Statement under article 19(1)" (Rule 46.4)

The amendments may be accompanied by a statement explaining the amendments and indicating any impact that such amendments might have on the description and the drawings (which cannot be amended under Article 19(1)).

The statement will be published with the international application and the amended claims.

It must be in the language in which the international application is to be published.

It must be brief, not exceeding 500 words if in English or if translated into English.

It should not be confused with and does not replace the letter indicating the differences between the claims as filed and as amended. It must be filed on a separate sheet and must be identified as such by a heading, preferably by using the words "Statement under Article 19(1)."

It may not contain any disparaging comments on the international search report or the relevance of citations contained in that report. Reference to citations, relevant to a given claim, contained in the international search report may be made only in connection with an amendment of that claim.

Consequence if a demand for international preliminary examination has already been filed

If, at the time of filing any amendments under Article 19, a demand for international preliminary examination has already been submitted, the applicant must preferably, at the same time of filing the amendments with the International Bureau, also file a copy of such amendments with the International Preliminary Examining Authority (see Rule 62.2(a), first sentence).

Consequence with regard to translation of the international application for entry into the national phase

The applicant's attention is drawn to the fact that, where upon entry into the national phase, a translation of the claims as amended under Article 19 may have to be furnished to the designated/elected Offices, instead of, or in addition to, the translation of the claims as filed.

For further details on the requirements of each designated/elected Office, see Volume II of the PCT Applicant's Guide.

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference SJK/BP5846076	FOR FURTHER ACTION see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. PCT/GB 00/01030	International filing date (day/month/year) 20/03/2000	(Earliest) Priority Date (day/month/year) 19/03/1999
Applicant UNIVERSITY OF ABERDEEN et al.		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 3 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

- a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

- b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing:

☐ contained in the international application in written form.

☐ filed together with the international application in computer readable form.

☒ furnished subsequently to this Authority in written form.

☒ furnished subsequently to this Authority in computer readable form.

☒ the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☒ the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. ☐ **Certain claims were found unsearchable** (See Box I).

3. ☐ **Unity of Invention is lacking** (see Box II).

4. With regard to the **title**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No.

☐ as suggested by the applicant.

☐ because the applicant failed to suggest a figure.

☐ because this figure better characterizes the invention.

☒ None of the figures.

INTERNATIONAL SEARCH REPORT

International Application No

CT/GB 00/01030

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07K16/40 C12N5/06 A61K47/48 G01N33/573 G01N33/574
G01N33/577 A61P35/00 C12N9/02

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07K C12N G01N A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

WPI Data, PAJ, MEDLINE, BIOSIS, EMBASE, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 97 12246 A (UNIVERSITY OF ABERDEEN) 3 April 1997 (1997-04-03) claims 1-26	1-19, 21-25
X	--- MURRAY G ET AL: "Tumor-specific expression of cytochrome P450 CYP1B1." CANCER RESEARCH (1997) 57 3026-31, XP002106430 page 3027, right-hand column, line 5 - line 13 --- -/--	1-18, 20-25



Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

* Special categories of cited documents:

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

T later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention.

X document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

Y document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

& document member of the same patent family

Date of the actual completion of the international search

22 June 2000

Date of mailing of the international search report

06/07/2000

Name and mailing address of the ISA

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NL - 2280 HV Rijswijk
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Fax: (+31-70) 340-3016

Authorized officer

Le Flao, K

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>TAILOR, G. ET AL: "Detection of cytochrome P450 CYP1B1 in human tumours using monoclonal antibodies against a C-terminal decapeptide." HUMAN & EXPERIMENTAL TOXICOLOGY, (SEPT., 1998) VOL. 17, NO. 9, PP. 534. MEETING INFO.: PROCEEDINGS OF THE BRITISH TOXICOLOGY SOCIETY ANNUAL CONGRESS GUILFORD, ENGLAND, UK APRIL 19-22, 1998 BRITISH TOXICOLOGICAL SOCIETY. , XP000914865 abstract</p> <p style="text-align: center;">---</p>	1-18, 20-25
X	<p>TANG Y M ET AL: "Development of an antipeptide antibody that binds to the C-terminal region of human CYP1B1." DRUG METABOLISM AND DISPOSITION, (1999 FEB) 27 (2) 274-80. , XP000914872 abstract page 276, left-hand column, line 15 - line 28</p> <p style="text-align: center;">---</p>	1-18
A	<p>MCKAY J ET AL: "Expression of cytochrome P450 CYP1B1 in breast cancer" FEBS LETTERS (1995) 374 270-2, XP000615313 page 271, right-hand column, line 15 - line 24; figure 4</p> <p style="text-align: center;">-----</p>	1-25

Information on patent family members

CT/GB 00/01030

Form PCT/ISA/210 (patent family annex) (July 1992)

INTERNATIONAL SEARCH REPORT

International Application No.

PCT/GB 00/01030

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"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance: the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

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"Z" document member of the same patent family

Date of the actual completion of the international search

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Date of mailing of the international search report

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Name and mailing address of the ISA

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A	<p style="text-align: center;">---</p> <p>MCKAY J ET AL: "Expression of cytochrome P450 CYP1B1 in breast cancer"</p> <p>FEBS LETTERS (1995) 374 270-2, XP000615313</p> <p>page 271, right-hand column, line 15 - line 24; figure 4</p> <p style="text-align: center;">-----</p>	1-25

INTERNATIONAL SEARCH REPORT

information on patent family members

International Application No

PCT/GB 00/01030

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9712246 A	03-04-1997	AU 7090396 A	17-04-1997
		EP 0856157 A	05-08-1998
		JP 11512818 T	02-11-1999
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